Notes on GIT medicine

Acute Upper GIT Bleeding

Definition: bleeding proximal to the ligament of Treitz.

Etiology: **Peptic ulcer** (Most common) > Mallory-Weiss syndrome > Gastritis, duodenitis. Esophagitis > Varices

Mallory-Weiss syndrome: It is a small longitudinal lesions at the gastro-esophageal junction. It occurs after repeated vomiting and causes a self-limiting bleeding

Clinical picture: **Hematemesis** **Melena:** [Tarry black, Offensive, Sticky stool]

- If severe bleeding → hypovolemic shock

Clues in History & Examination for the cause:

History: • H/O alcohol intake • Drug H (NSAIDs, Corticosteroids, anti-coagulants)

Physical examination: Look for stigmata of chronic liver disease

- Presence of telangiectasia on the face and lips or mouth suggest hereditary telangiectasia which affects all of the GIT & may be the cause of bleeding.

Management

- Call for HELP + Stabilize the patient ABC:
  - A→ Give high-concentration Oxygen
  - B→ Assess breathing by counting the respiratory rate
  - C→ Insert 2 large IV cannula and start infusing fluid and Take blood for:
    - **CBC** (for base line hemoglobin)
    - **Urea** and **Electrolyte**: Urea may be ↑ due to increased protein in the GIT from the digested RBC and due to hypovolemia.
    - **Blood group** and **Urgent Cross matching** (at least 4 units initially)
    - **Clotting Factors** [especially in pts on anticoagulants or with liver disease]
  - Indications for blood transfusion are: **SHOCK** OR **Hemoglobin < 10g/dl**

➢ *Identify the source of the bleeding & Treatment*

- **Endoscopy is the investigation of choice** because its Diagnostic & Therapeutic

Endoscopic Rx
- Gastritis. Duodenitis. Esophagitis. Mallory-Weiss syndrome → Conservative Rx
- **Peptic ulcer + CA** → Adrenalin injection
  - → Heater probe or Laser photocoagulation

Esophageal varices

1. Endoscopic band ligation or sclerotherapy is the **Procedure of choice**
2. Medical treatment: Terlipressin (Vasopressin) Or Octreotide
3. Sengstaken-Blakemore tube if uncontrolled hemorrhage
4. Transjugular Intrahepatic Portosystemic Shunt (TIPS) if above measures fail

Investigations for patient with liver disease

1. Serum Aminotransaminases

- Aspartate aminotransaminase (AST) = serum glutamic-oxaloacetic transaminase (SGOT)
- Alanine aminotransaminase (ALT) = serum glutamic-pyruvic transaminase (SGPT)
- Released during hepatocyte plasma membrane damage
- Normal levels of ALT and AST is **< 40 IU**, raise of **< 6 time** the normal is not specific [i.e. may be cholestatic or hepatitic], but raise of **> 6 times** the normal is going with hepatitic liver disease
- AST/ALT > 2 suggests alcoholic liver disease
- ALT is more specific for liver than AST which found in muscles and RBCs.

2. Alkaline Phosphatase

- Found in Liver, Bone, Intestine, Placenta, Leukocytes
- Normal levels **45–115 U/L**, elevation of **< 2.5** time in serum ALP values is not specific but elevation of **> 2.5** time in serum ALP occurs in cholestatic liver disease
- The half-life of serum ALP is 7 days.

3. Albumin

- Most abundant protein synthesized by liver
- Half life = 20 days
- Insensitive to mild injury [**So if Albumin is ↓ = Chronic Sever liver disease**]
- May be affected by nutrition, GIT and renal losses
- When reduced → edema and ascites

4. Prothrombin Time

- Except for factor VIII, all blood clotting factors are made only in liver.
- The serum half-lives are shorter than albumin [hours] → so it is the single best measure of acute ↓ in hepatic synthetic function.
- Normal PT is (11–13 sec)

5. **Bilirubin:** Normal bilirubin levels (0.0–1.0 mg/dL) [1mg = 17 μmol]

Bilirubin production and metabolism:

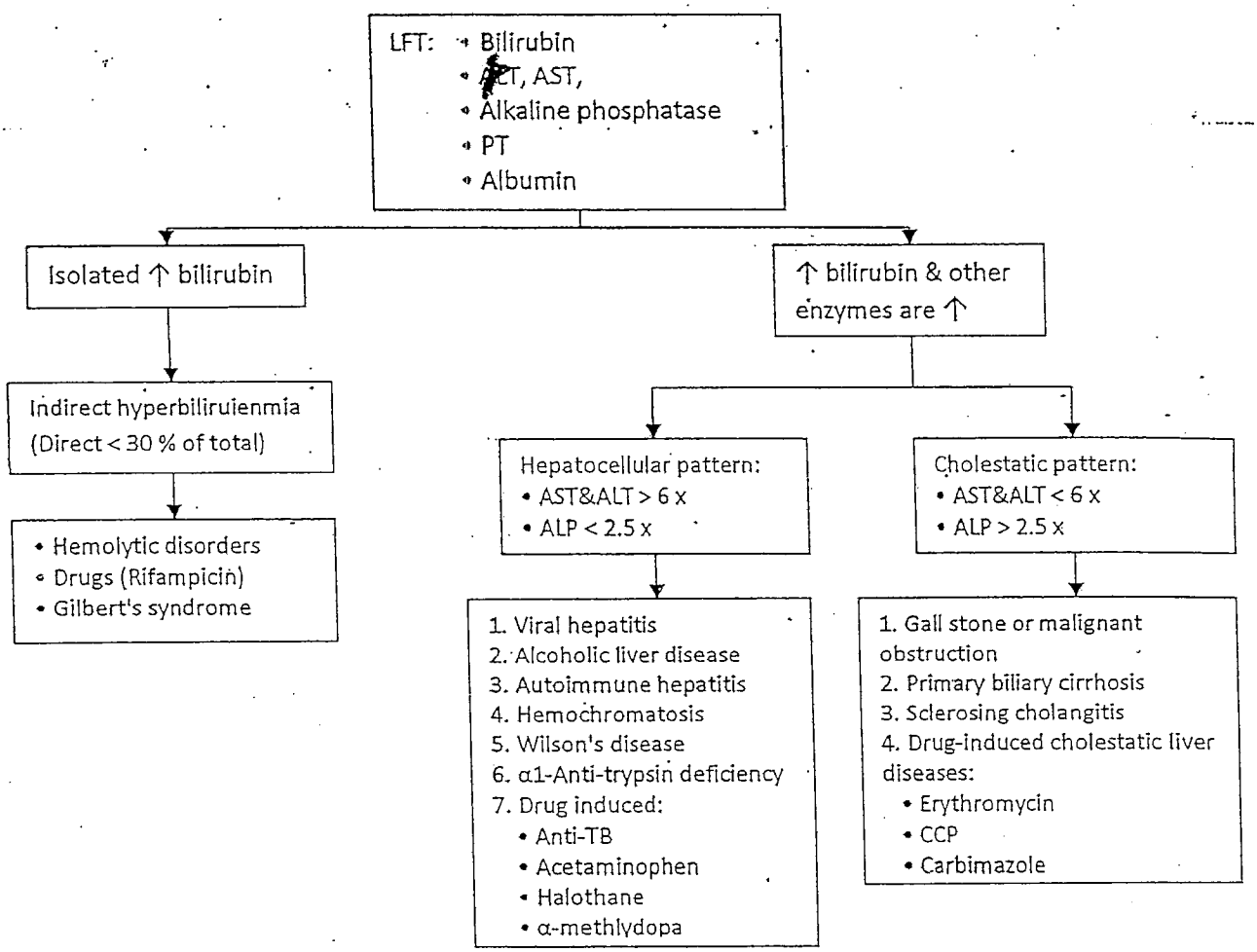
- Bilirubin is a breakdown product of heme from dead RBCs.
- The formation of bilirubin occurs in the spleen and liver. And the bilirubin formed is insoluble in water and called (**Unconjugated bilirubin**).
- Unconjugated bilirubin binds to albumin to be transported to the liver, where it is taken up by hepatocytes where it is conjugated to glucuronic acid to produce (**Conjugated bilirubin**) which is water soluble.
- The conjugated bilirubin is excreted into bile which drains into the duodenum and passes unchanged through the proximal small bowel. When the conjugated bilirubin reaches the distal ileum and colon, it is hydrolyzed to unconjugated bilirubin by bacterial–glucuronidases to form urobilinogen. About 90% of urobilinogen are excreted in feces and are called stercobilinogen. The remaining 10% of the urobilinogen is absorbed, and enters the portal venous blood, and is reexcreted by the liver. A small fraction escapes hepatic uptake, filters across the renal glomerulus, and is excreted in urine and called urobilinogen.
- So the presence of urobilinogen in urine excludes biliary obstruction as a cause.

Correlation between the level of the bilirubin and the underlying cause:

- In hemolysis unconjugated bilirubin level is < 5 mg/dL
- Bilirubin levels > 20 mg/dL suggest malignant biliary obstruction.

Other tests:

- *Gamma-glutamyl Transpeptidase (GGT) + 5'-Nucleatidase* Both are used to determines if elevated ALP is due to liver disease
- *GTT* is also elevated also in Alcoholic pts



Approach to Pt with jaundice

MC: Dark urine & pale stools & itching indicate cholestasis. Dark urine may occur if the cause if hemolysis.

PMHx: Surgery & Anesthesia [halothane], Blood transfusion (hepatitis B or C)

Family Hx: [Hemolytic anemia, Hemochromatosis, Wilson's disease, α1-Anti-trypsin deficiency]

Social Hx: Alcohol, Risk factors for viral hepatitis [Sexual history (A,B,C), Tattoo, Drug abuse], Travel (hepatitis, amoebiasis)

Drug Hx: Anti-TB, Acetaminophen, Oral contraceptive…etc

Liver Cirrhosis

Definition: A disease of the liver that is characterized by fibrosis, disorganization of the lobular and vascular architecture, and regenerating nodules of hepatocytes.

Etiology

- Viral hepatitis (B, C, D)
- Alcoholic liver disease
- Primary biliary cirrhosis • Autoimmune
- Genetic: Primary hemochromatosis • Wilson disease • α_1-Antitrypsin deficiency
- CHF (Cardiac cirrhosis)
- Cryptogenic cirrhosis 10%

Investigations

- **CBC:** Anemia (microcytic due to blood loss), Pancytopenia (hypersplenism).
- **RBS:** may show hypoglycemia.
- **Coagulation test:** Prolonged PT.
- **Urea and electrolyte:** hyponatremia.
- **ABG:** hypokalemic alkalosis, hypoxemia (hepatopulmonary syndrome).
- **Blood protein:** hypoalbuminemia (albumin level < 3.5 g).
- **Liver biopsy** is the gold standard for the Dx of cirrhosis, but the Dx is usually made on C/P & Other investigations & biopsy is done for difficult cases only

Morphology → Macronodular > 3mm → Post-hepatitis
Morphology → Micronodular < 3 mm → Alcoholic + Hemochromatosis

Diagnostic tests in liver disease	
Disease	**Diagnostic Test**
Hepatitis A	Anti-HAV IgM
Hepatitis B	
Acute	HBsAg and anti-HBc IgM
Chronic	HBsAg and HBeAg and/or HBV DNA
Hepatitis C	Anti-HCV and HCV RNA
Hepatitis D (delta)	HBsAg and anti-HDV
Hepatitis E	Anti-HEV
Autoimmune hepatitis	**ANA** (Anti-Nuclear Antibodies) ↑ IgG and biopsy
Primary biliary cirrhosis	**AMA** [Anti-Mitochondrial Antibody], ↑ IgM levels and biopsy
Alcoholic liver disease	History of alcohol intake (IgA may be raised) and biopsy
α_{-1} Antitrypsin disease	Reduced α_{-1} antitrypsin levels
Wilson disease	↓ Serum Ceruloplasmin. ↑ Urinary copper. ↑ Liver copper
Hemochromatosis	↑ Serum ferritin + Genetic test for *HFE* gene mutations

Complications

1. Portal hypertension → Ascites which may → Spontaneous bacterial peritonitis
   → Esophageal varices
   → Splenomegaly which may → Pancytopenia
2. Systemic effects → Hepatic encephalopathy
   → Hepatorenal syndrome
   → Hepatopulmonary syndrome
3. Others → Bleeding tendency
   → Malnutrition
   → Hepatocellular carcinoma

Hepatic Encephalopathy

Definition: A state of disordered CNS function associated with severe acute or chronic liver disease; may be acute and reversible or chronic and progressive.
There is a characteristic EEG abnormality which correlate with clinical stage.

Clinical presentation

Stage 1: euphoria or depression, mild confusion, slurred speech, disordered sleep (cycle reversal)
Stage 2: lethargy, moderate confusion.
Stage 3: marked confusion, sleeping but arousable, inarticulate speech.
Stage 4: coma; initially responsive to noxious stimuli, later unresponsive.

Sign: Flapping tremor are present unless the pt is unconscious. Fetor hepaticus

Pathophysiology

- Failure of liver to detoxify agents harmful to CNS e.g. Ammonia, GABA, Mercaptan, Fatty acids.
- Note: Blood ammonia is ↑ but the ↑ doesn't correlate with clinical status.

Precipitant factors

1. GI bleeding (100 mL = 14–20 g of protein)
2. Constipation
3. High-protein meal

Treatment

- Remove precipitants. Reduce blood ammonia by decreasing protein intake
- Lactulose oral (converts NH3 to unabsorbed NH4, produces diarrhea, alters bowel flora). In coma, it is give as enema.
- In refractory cases, add neomycin, metronidazole, or vancomycin.
- Liver transplantation if indicated.

CBC interpretation

Hematological values	
Index	Range
White blood cell (WBC)	4 -11 x10^9/l
Hemoglobin, male	130-170 g/l (13-17 g/dl)
Hemoglobin, female	120-160 g/l (12-16 g/dl)
Mean cell volume (MCV)	80-100 fl
Mean cell hemoglobin (MCH)	27-32 pg
Mean cellular hemoglobin concentration (MCHC)	31-35 g/dl
Red cell distribution width (RDW)	11.5-15
Platelets	150-400 x10^9/l

Investigations In hematology

Complete Blood count

It includes: Hemoglobin, Hematocrit, WBC num, RBC num, Platelet num, Reticulocyte count, & Blood indices [MCV, MCH, MCHC]

Hematocrit value = packed cell volume (PCV):

- It is the volume of packed RBCs in 100 ml blood.
- It is not affected in acute bleeding except after about 12 hours until hemodilution occur.
- ♂ = 40 – 54% ♀ = 37 – 47%
- It ↓ with anemia and ↑ with polycythemia

Blood indices

- Blood indices are average numbers

Mean corpuscular Hb = MCH

- It is the amount of Hb per cell = 27 - 32 pg/Ery
- Hypochromia → M.C.H < 27 pg/Ery
- Hyperchromia → *MCH* ≥32 pg/Ery

Mean corpuscular volume = MCV

- It is the mean volume of one cell.
- ↑ in Macrocytosis (MCV > 100 fL)
- ↓ in Microcytosis (MCV < 80 fL)
- Normal in normocytic anemia

Mean corpuscular hemoglobin concentration = MCHC

- It is the Concentration of Hb in the red cell = 31 – 35%
- The MCHC is similar to MCH as it reflect defects in hemoglobin synthesis

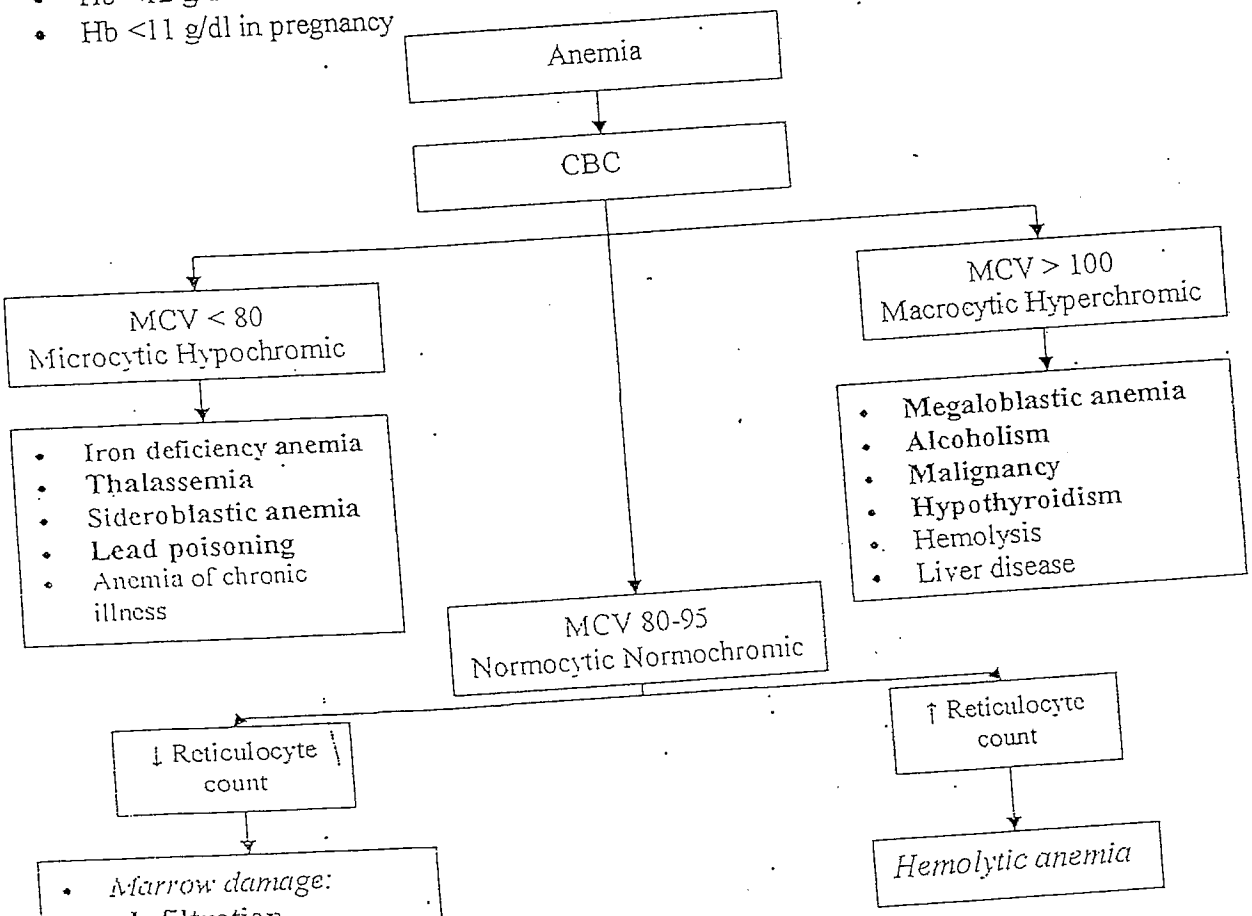
Reticulocyte count

- Since the lifespan of circulating erythrocytes is about 120 days. reticulocytes constitute slightly less than 1% of circulating red blood cells.
  - Reticulocytes are young RBCs newly released from the marrow. They can be detected by their lacy network of RNA.
  - They are slightly larger and bluer than mature RBC.
- **Reticulocytosis indicates hemolysis or loss of blood.** [Other causes of Reticulocytosis are response to treatment of iron, folate, or vitamin B_{12} deficiency].
- **Reticulocytosis indicates an active marrow (normal marrow function)**
- If the reticulocyte count is low, a primary marrow disorder should be considered.

Anemia

According to WHO criteria anemia is defined as:

- Hb <13 g/dL in adult male.
- Hb <12 g/dL in adult females.
- Hb <11 g/dl in pregnancy



Pathophysiology

- **Hypochromic microcytic anemia:** the erythropoietic stem cell kinetics and DNA synthesis are normal, but cytoplasmic synthesis of hemoglobin is impaired.
- **Macrocytic Hyperchromic anemia:** the erythroid precursors cannot produce nucleic acid, and so nuclear maturation is arrested. While Cytoplasmic maturation proceeds, resulting in abnormally large cells.
- **Normocytic Normochromic anemia:** here the RBCs are generally normal in morphology but too few are produced.

Iron deficiency anemia

Epidemiology

- in men & postmenopausal women the **most common cause is GIT Bleeding.**

Iron metabolism

Iron daily requirement
- → ♂ + post menopausal ♀ = 1 mg
- → Menstruating ♀ = 1.5 - 2 mg
- → Pregnancy = 5-6 mg

- Absorption:
  - Iron is absorbed from the duodenum & upper jejunum.
  - Ferrous iron (Fe^{2+}) is more absorbable than ferric iron (Fe^{3+})
  - Absorption is ↑ by acids (*gastric acid/ascorbic acid*) & ↓ by *tannates*d in tea.
- Iron is transported by **transferrin** & stored as **ferritin** in liver &bone marrow
- In iron ↓ anemia iron stores ↓ →. ↓ ferritin.

Etiology

- Chronic blood loss → GIT (Common causes):
  - Hiatus hernia (*Cameron ulcer*)
  - Peptic ulcer (pts on NSAID or Steroid).
  - IBD
  - CA stomach, colon.
  - → Menstruation
  - → Urinary tract
- ↓ Intake: Pt not eating meat. [vegetarian pt eat iron but in no-absorbable form].
- Malabsorption:
  - ↓ Gastric acid: Post-gastrectomy
  - Small intestinal disease e.g. Celiac
- ↑ Demand: in children, pregnancy and lactation

Clinical features

Symptoms of anemia[↓ O_2]
- Muscles → Fatigue = Tiredness = Lassitud
- CNS → Headache
  - → Lightheadedness & Fainting
- Resp sys → Dyspnea on exertion
- Cardiovascular Sys → Palpitation
  - → In pt with heart disease:
    - Symp of CHF: LLE
    - Angina

Sings

- Skin and mucous membranes pallor [hemoglobin level is 8–10 g/dL]
- Palmar creases pallor [hemoglobin level is < 8 g/dL]
- Glossitis (smooth. red tongue), painless stomatitis, and angular cheilitis.
- **Koilonychia**: spooning of the fingernails. [in Ch. iron deficiency anemia]
- Tachycardia and systolic ejection murmur

Investigations

- **CBC** (Microcytic Hypochromic anemia):
  - ↓ Hb, ↓ Hct, ↓ RBCs count.
  - The MCV < 80 fl (**microcytic**), & MCH < 27 pg (**hypochromic**).
  - ↑ Platelet count suggests bleeding as a cause.
  - High RDW (Red Cell Distribution Width) denoting **anisocytosis**
- **Iron studies**: Serum iron, transferrin saturation (TIBC), and Transferrin saturation
  1. Serum ferritin is low:
     - Due to reduced or absent body iron stores.
     - Serum ferritin is the best single test to confirm iron deficiency
  2. Serum iron is low.
  3. Total iron capacity (TIBC) (Transferrin level) is high
  4. Transferrin saturation is the ratio of serum iron to TIBC.
     - In Fe-deficiency it is decreased to < 16%. [normally > 30%]
- **Investigations for the etiology**: As stool analysis &Upper & Lower GI endoscopy.

Management

1. Correct underlying disorders
2. **Oral preparation** is the best treatment route.
   - Ferrous sulphate [dose 200 mg of elemental iron daily].
   - Ferrous sulphate tablet contains 65 mg of elemental iron→ given 3 times/ day.
   - SE: Black stool, Diarrhea, Constipation
   - Treatment is continued for 3 months after the hemoglobin has returned to normal to replenish iron stores.
3. **Parenteral preparations** (IM or IV) are used only is in pts who are unable to tolerate oral therapy or pt with malabsorption or continuing severe blood loss.
   - Parenteral route is associated hypersensitivity reactions.(anaphylaxis).
   - Parenteral route does not lead to more rapid repair of anemia.
   - Preparations→Iron sorbitol given deep IM by Z-technique [SE: Painful & causes brown skin discoloration at site of injection]
4. **Blood transfusion:**
   a. Only if pt is severely symptomatic or to prepare the patient for surgery.
   b. Pt with Hb < 8g/dl is likely to need blood transfusion.
   c. In pt with heart failure give packed RBC.

Monitoring response to iron therapy:

1. Reticulocytosis starts on 3rd day & peaks at 7th after starting treatment.
2. Hemoglobin rises by rate of 1g/dl per week.
3. Normalization of the hemoglobin level (1 month)
4. Repletion of iron stores (2-4 months).

If the pt is not responding look for another cause of anemia.

Megaloblastic Anemia

Definition: A group of anemias caused by deficiency of B_{12} or Folic acid.

	Vit B_{12}	Folic acid
Metabol	• Requirements: 1 micro gm/d. • Sources : Animal sources • Absorption: Ileum • Store: 3-5 mg in liver can supply for 5 yr	• Requirements: 50 micro gm/d • Sources: Animal and Vegetables. • Absorption: duodenum and Jejunum. • Stores: 5-15 mg, can supply for months.
Causes	1. ↓ Intake: rare & occurs in vegetarians. 2. ↓ Intrinsic factor: Pernicious anemia (most common cause) 3. Intestinal disease: ▪ Ileal disease e.g. Crohn's disease ▪ Bacterial overgrowth syndrome ▪ Diphyllobothrium latum.	1. ↓ Intake (common in alcoholics, elderly) 2. Intestinal disease e.g. Celiac disease . 3. ↑ demand (pregnancy) 4. Drugs: a. Phenytoin b. Methotrexate c. Azathioprine

Note on absorption of Vit B 12: Parietal cells of stomach secrete an **intrinsic factor** which combines with Vit. B_{12}. → On reaching the terminal ileum the B_{12} – intrinsic factor complex where it is absorbed → after absorption Vit. B_{12} binds to **transcobolamin II** to be transported to tissues.

Clinical Picture

- Symptoms & signs of anemia
- **Neurological manifestations occur only in Vit B_{12} deficiency:**
  - Subacute combined degeneration = Posterior column + Pyramidal tracts.
  - Cerebral: dementia, psychosis (megaloblastic madness), optic atrophy
  - Peripheral neuropathy

Investigations

- **CBC:** (Macrocytic, Hyperchromic)
  - ↓ Hb, Hct, & RBC
  - MCV >100 (macrocytic anemia)
  - ↓ WBC (neutropenia) & ↓ Platelets (thrombocytopenia) may occur
  - Reticulocyte count is low but increases with treatment.
- **Peripheral blood film: Hypersegmented neutrophils.**
- **Lab:** ↑ Serum bilirubin & ↑ LDH due to intramedullary haemolysis
- **Folate deficiency Dx:** measurements of Red cells folate.
- **Vit B_{12} deficiency Dx:** ↑Methylmalonic acid levels &Vit B_{12} serum levels

Schilling test: it tests for the presence of intrinsic factor and intestinal function to find out the cause of vitamin B_{12} deficiency. **Procedure:** Vit B_{12} is given I.M. to saturate stores then give B_{12} orally labeled with radioactive material, normal person secrete radioactive B_{12} in urine but Pt with pernicious anemia (no intrinsic factor will not absorb Vit B_{12}. If intrinsic factor the pt will absorb Vit B_{12}.

Treatment

1. Vit B_{12} deficiency: **IM Hydroxycobolamine.**
2. Folate deficiency: **Oral folic acid.**

Hemolytic anemia

Overview

- Hemolysis = RBC life < 120 days.
- BM can ↑ production of RBC by 8 times, but when it fails to compensate → anemia

Physiology of red cell destruction

- Extravascular hemolysis
  - In Extravascular hemolysis the RBC are removed by macrophages of the reticuloendothelial system mainly in spleen → **Splenomegaly**.
  - Breakdown of Hb → ↑ unconjugated bilirubin → **Jaundice**.
  - The ↑ bilirubin will be excreted by liver → ↑ risk of **pigment stones**.
    → ↑ urine Urobilinogen [not bilirubin]
- Intravascular hemolysis
  - Intravascular destruction indicates fragmentation of RBC within in the circulation.
  - Hb released bind to proteins called **Haptoglobins**, and they from a complex removed by the liver, so in hemolytic anemia Haptoglobin level is **Decreased.**
  - When the binding capacity of haptoglobin is exceeded, free hemoglobin is filtered in the kidney and converted to hemosiderin in renal tubular cell →**Hemosiderinuria** After that **Hemoglobinuria** (hemoglobin in the urine) → Black urine.

Clinical picture → Anemia
→ Jaundice
→ Splenomegaly

Causes of hemolytic anemias

Congenital	Acquired
• Membrane defects 1. Spherocytosis 2. Elliptocytosis • Hemoglobinopathies 1. Sickle cell disease 2. Thalassemia • Red cell enzyme defects 1. G6PD deficiency 2. Pyruvate kinase deficiency	• Autoimmune 1. Infections: EBV, Mycoplasma 2. Systemic lupus erythematosus **SLE** 3. Chronic lymphocytic leukemia **CLL** • Non-immune 1. Microangiopathic hemolytic anemia 2. Prosthetic heart valve 3. Drug- or toxin-induced

Investigation	
Hemoglobin	↓
MCV, MCH	Normocytic or Macrocytic
Reticulocytes	↑ **Reticulocytosis**
Bilirubin	↑
LDH	↑
Haptoglobin	Reduced to absent
Blood film	Polychromasia [↑ retculocytosis]

Potassium disorders

Normal plasma K^+ = **3.5-5.0 mmol/L**. [< 3.5 is Hypokalemia] [> 5 is Hyperkalemia]
- Abnormal K^+ levels can → cardiac arrhythmia or arrest = Death

Regulation of potassium metabolism
- Absorption → GIT
- Excretion → Kidney [Aldesterone acts on the collecting duct it ↑ Na^+ reabsorption & ↑ K^+ excretion]
- K^+ shift across the cell membrane (affected by 3 factors):
  1. **Insulin** → ↑ shift of K^+ into cells.
  2. **β_2-Adrenergic agonists** → ↑ shift of K^+ into cells.
  3. **PH**: Alkalosis → ↑ shift of K^+ into cells X Acidosis → Shift out of cell

	Causes of hypokalemia and hyperkalemia	
	Hypokalemia	**Hyperkalemia**
	GIT loss → Vomiting OR Diarrhea	*Increases intake* → Intravenous K^+
	Renal loss • Diuretics (Thiazide, Furosemide) • ↑ Aldesterone • ↑ Corticosteroids	*Renal retention* • Renal failure • Hypoaldosteronism: 1. Adrenal disease 2. ACE inhibitors 3. Spiranolactone
	Shift into the cells • Metabolic alkalosis • β-agonists • Insulin excess or overdose	*Shift out of cells* • Metabolic acidosis • β-blockers • Insulin deficiency (DKA) • Pseudohyperkalemia (in vitro hemolysis)
C/P	Muscle weakness, Constipation Arrhythmia [AF & VF] ↑ Digitalis toxicity	Muscle weakness Arrhythmia [VF]
Ix	Serum K^+ levels, ECG: U wave.	Serum K^+ levels, and ECG: • Widening of the QRS • Tall T waves
Rx	Oral or IV K^+ [The rate of infusion should be < 20 mmol/h. because K^+ has to pass from ECF to ICF].	See below

Treatment Hyperkalemia: Call for help & Do an ECG
1. Give **10 ml 10% calcium gluconate** if there are ECG changes; repeated every 10 to 20 mins until ECG normalizes. It doesn't ↓ K^+ level but it stabilizes the myocardium
2. Give **50% dextrose 50 ml + soluble insulin 10 units**: shifts K^+ into cells
3. **Sodium bicarbonate** → temporary alkalosis → intracellular shift of K^+
4. **Furosemide** combined with hydration encourages renal excretion.
5. **Calcium resonium** oral or rectally. It ↑ K^+ excretion from gut
6. Hyperkalemia + renal failure = **dialysis**

Calcium disorders

- The three organs involved in calcium homeostasis are the bone (storage), kidney (excretion), and intestine (absorption).
- The three hormones involved in calcium homeostasis are parathyroid hormone, vitamin D, and calcitonin.
- Parathyroid hormone and vitamin D work to increase calcium levels. ↑
- Calcitonin decreases calcium levels. ↓

Causes	
Hypercalcemia	Hypocalcemia
1. Hyperparathyroidism: Primary OR Tertiary 2. Malignancy Multiple Myeloma, 3. Vit D excess: ↑intake OR increased formation: granulomatous disease: sarcoidosis & TB 4. Thiazide	1. Hypoparathyroidism 2. Vit D deficieney 3. Renal failure Acute or Chronic

Clinical features	
Hypercalcemia	Hypocalcemia
Polyuria & Polydepsia Arrhythmias Dehydration GIT: • Constipation •Pancreatitis Renal: • Stones • Nephrocalcinosis	Perioral and peripheral numbness Carpal-pedal spasm Tetany may → Laryngospasm Manifest due to Neuromuscular Seizures Chvostek's sign latent Trousseau's sign latent prolonged QT interval

osmotic diuretic ↓ Kidney + Bone ↓ Intestinal

peptic ulcer ↓ level of consciousness

Management of Hypercalcemia

Mainly in Emergency

- Rehydrate patient with iv N saline (0.9%).
- Diuretics: once patient is rehydrated, continue N saline infusion and add frusemide
- Bisphosphonates inhibit osteoclast activity thereby causing a fall in plasma Ca^{2+}. [e.g. Pamidronate, or Zolendronate]
- Calcitonin
- Steroids: Most effective in sarcoidosis, and malignancies
- If the pt has renal failure consider dialysis

↑ Ca Lung ↑ hypercalcemia in absence of Metastasis

Rx of hypercalcemia

Acute calcium gluconate 10ml 10% 10 min

Akram M.F. Alkrekshi

- Chronic

Acute complications of DM

Diabetic Ketoacidosis & Hyperosmolar Hyperglycemic state

- DKA is seen mainly type 1 DM and HHS mainly in type 2 DM.
- Both disorders are associated with absolute or relative insulin deficiency, volume depletion, and altered mental status.

Laboratory Changes in DKA and HHS		
	DKA	HHS
Glucose	250-600	600-1200
Sodium	125-135	135-145
Potassium	Normal or ↑	Normal
Chloride	Normal	Normal
Phosphate	↓	Normal
Osmolality (mOsm/ml)	300-320	330-380
Plasma ketones	++++	Normal or Slightly +
Arterial pH	6.8-7.3	> 7.3
Arterial Pco_2	20-30	Normal
Anion gap	↑	Normal to slightly ↑

Diabetic ketoacidosis

Etiology: DKA results from severe insulin deficiency with ↑ in glucagons.

Causes

1. Inadequate insulin administration
2. Infection (pneumonia, UTI, gastroenteritis, sepsis)
3. Infarction (cerebral, coronary, mesenteric, peripheral)
4. Surgery
5. Drugs (cocaine)

Clinical feature

- Polyuria, Polydepsia, & weight loss.
- Anorexia, nausea, vomiting, and abdominal pain.
- Vital signs: ↑ HR, ↓ BP, ↑ RR, ± Fever
- Kussmaul respirations and an acetone odor on the pt's breath.
- Altered mental function, or even coma.

Investigations: reveals hyperglycemia, ketosis (β-hydroxybutyrate, & acetoacetate), and metabolic acidosis (arterial pH 6.8–7.3).

- Despite a total-body potassium deficit, the serum potassium at presentation may be normal or mildly high as a result of acidosis.
- Leukocytosis is common.
- The measured serum sodium is reduced as a consequence of hyperglycemia.

Management of DKA

1. **Confirm diagnosis** (plasma glucose, positive serum ketones, metabolic acidosis)
2. **Admit to hospital.**
3. **Initial assessment:** Serum Urea & Electrolytes & ABG
4. **Replacement**
   a. **Fluids:**
   - 0.9% saline (NaCl) I.V
     - 1 liter over 30 minutes
     - 1 liter over 1 hr
     - 1 liter over 2 hrs
     - 1 liter over next 4 hrs
   - When blood glucose 270 mg/dl
     - Switch to 5% dextrose, 1 liter 8-hourly
   - Typical requirement is 6 liters in first 24 hrs.

   b. **Electrolyte (K):**
   - Potassium chloride should be added to each liter of i.v. fluid as follows:
     - 20mmol if plasma potassium is normal (3.5-5.0mmol/L).
     - 40mmol in hypokalaemia (<3.5mmol/L).
     - none in hyperkalaemia (>5.0mmol/L).

   c. **Sodium bicarbonate** (1.4%): may be given if arterial pH is 6.9 or less.

5. **Administer regular insulin:**
- 50 units soluble insulin in 50 ml 0.9% saline I.V. via infusion pump
  - 6 units/hr initially
  - 3 units/hr when blood glucose < 15 mmol/l (270 mg/dl)
  - 2 units hr if blood glucose declines < 10 mmol/l (180 mg/dl)
- If initial serum potassium is < 3.3 mmol/L , do not administer insulin until the potassium is corrected to > 3.3 mmol/L

7. **Monitoring:**
   - Measure capillary glucose every 1–2 h.
   - Measure electrolytes (especially K^+, bicarbonate) & ABG every 4 h for first 24 h.
   - BP, pulse, respirations, mental status, and fluid intake &output every 1–4 h.
6. **Investigate for the cause.**
7. Administer intermediate or long-acting insulin as soon as patient is eating. Allow for overlap in insulin infusion and subcutaneous insulin injection.

Complications of DKA

1. Cerebral edema [it has high mortality, more in children, associated with rapid reduction of blood glucose and use of bicarbonate, and is Rx with mannitol]
2. Acute respiratory distress syndrome
3. Thromboembolism
4. Disseminated intravascular coagulation (rare)
5. Acute circulatory failure

Prognosis

- Overall mortality is 10%, but it exceeds 20% in older patients.

Hyperglycemic Hyperosmolar State

Etiology

- Relative insulin deficiency and inadequate fluid intake are the causes of HHS.
- Hyperglycemia → osmotic diuresis → profound intravascular volume depletion.
- HHS is often precipitated by a serious, concurrent illness such as MI or sepsis.
- Hyperketonaemia does not develop because these patients have enough insulin secretion to suppress lipolysis and ketogenesis, but not enough to prevent the liver from producing glucose.

Clinical features

- Usually the pt is an elderly individual with polyuria, thirst, weight loss ± ↓ level of consciousness.
- Symptoms of nausea, vomiting, and abdominal pain and the Kussmaul respirations characteristic of DKA are ABSENT.

Investigation (see table above)

- In contrast to DKA, acidosis and ketonemia are usually not found; however, a small anion gap may be due to lactic acidosis, and moderate ketonuria may occur from starvation.
- The measured serum sodium is normal or slightly low.

Treatment

- The precipitating problem should be sought and treated.
- The management is similar to DKA but **Half the dose of insulin**, because the pts are more sensitive to insulin.

Prognosis

- High mortality rate (40%) due to the presence of other disease such as ischemic heart diseases in these pts.

ABG (Arterial blood gas)

Introduction:

- An arterial blood gas (ABG) test measures the acidity (pH) and the levels of oxygen and carbon dioxide in the arterial blood. The usual site is *radial artery*; and Allen test should be done before taking the sample.
- The body is continually producing acid as a byproduct of metabolism. And pH must be maintained in a narrow range for normal enzymatic activity. This narrow range of pH values is maintained by buffers.
- There are many buffers that help prevent sudden changes in the intracellular pH (such as bicarbonate, phosphate, hemoglobin). The most important buffer system in is the carbonic acid-bicarbonate system $H_2O+CO_2 <-> H_2CO_3 <-> HCO_3^- + H^+$
- The bicarbonate system is used to regulate the whole-body pH because it is possible to regulate it at two different sites: **HCO_3 is regulated by the kidneys** and **CO_2 is regulated by the lungs.**
- CO_2 is an acid while HCO_3 is an alkali.
- **Acidosis** is due to gain of acid or loss of alkali; causes may be metabolic (↓ serum HCO_3) or respiratory (↑ PCO_2). **Alkalosis** is due to loss of acid or addition 2 of base and is either metabolic (↑ serum HCO_3) or respiratory (↓P CO_2).
- **Compensation**: to limit the change in pH, metabolic disorders evoke an immediate compensatory response in ventilation; compensation to respiratory disorders by the kidneys takes days. But **the body never overcompensates,** for e.g. a metabolic acidosis will drop the pH to <7.4. If there is respiratory compensation the pH will return towards normal but will not overshoot to become >7.4.

Indications for ABG:

I-Respiratory Diseases

1. Severe pneumonia
2. Status Asthmatics
3. Acute bronchiolitis
4. Respiratory failure

II-Cardiac Diseases → Severe HF

III-Metabolic Diseases (Electrolytes)

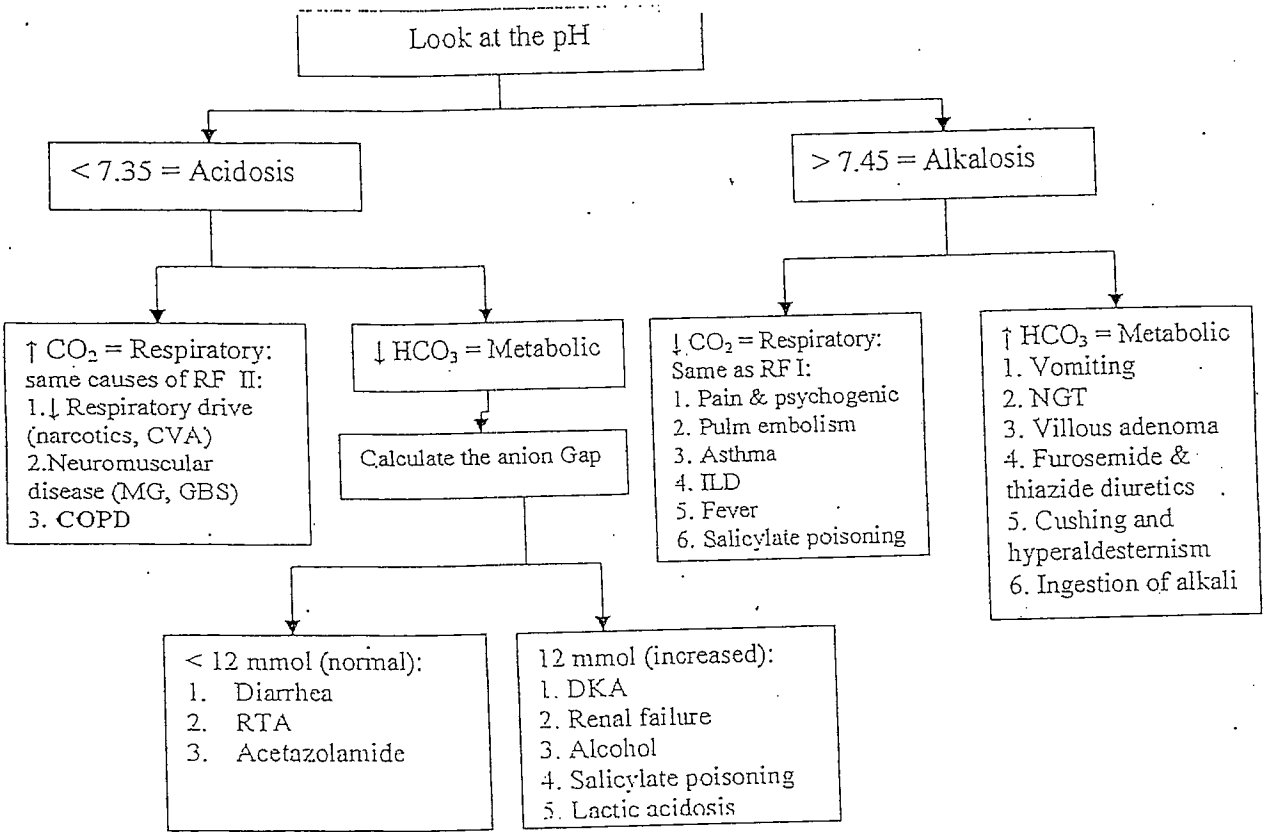
1. Renal Failure
2. DKA

IV-Poisoning → Salicylates

Normal values	Abnormalities	
pH = 7.35 – 7.45	<<7.35 = Acidosis	>7.45 = Alkalosis
PO2 = 80 – 100 mmHg	< 80 mmHg → hypoxemia < 60 mmHg → respiratory failure	
PCO2 = 35 – 45 mmHg	< 35 = Hyperventilation > 45 = Hypoventilation > 50 = Respiratory failure	
HCO3 = 18 – 28 mEq/L		

Analysis of ABG:

1. Look at pH. This tells you the primary acid-base abnormality. The body never overcompensates
2. Next, look at the arterial carbon dioxide tension ($Paco_2$) and standard bicarbonate to find out if this is a respiratory or metabolic problem
3. Measure the anion gap in any metabolic acidosis



Metabolic acidosis

The low HCO_3 results from the addition of acids (organic or inorganic) or loss of HCO_3.
Anion gap = Na^+ - (Cl^- + HCO_3) = (normally <12 mmol/L)
Investigations: Diagnosis may be made by measuring BUN, creatinine, glucose, lactate, serum ketones, and serum osmolality and obtaining a toxic screen.
Clinical features: hyperventilation, cardiovascular collapse, and ↓ level of consciousness
Treatment

- Always correct the underlying disturbance
- Na-bicarbonate

Metabolic alkalosis

- May occur in hyperaldosteronism due increased H^+ secretion

Treatment

- Rx underlying cause
- Severe alkalosis may require addition of acidifying agents such as NaCl, or acetazolamide.

Respiratory acidosis

Treatment: Rx underlying respiratory cause

Respiratory Alkalosis

Clinical feature are those of hypocalcemia due to shift of calcium from ionized active form to non-ionized non-active form → clinical picture of hypocalcemia.
Treatment

- Rx underlying respiratory cause
- In psychogenic cases, sedation or a rebreathing bag may be required.

Status Epilepticus

Definition: it is a prolonged seizure [> 30-minute] or repetitive seizures without a return to baseline consciousness.

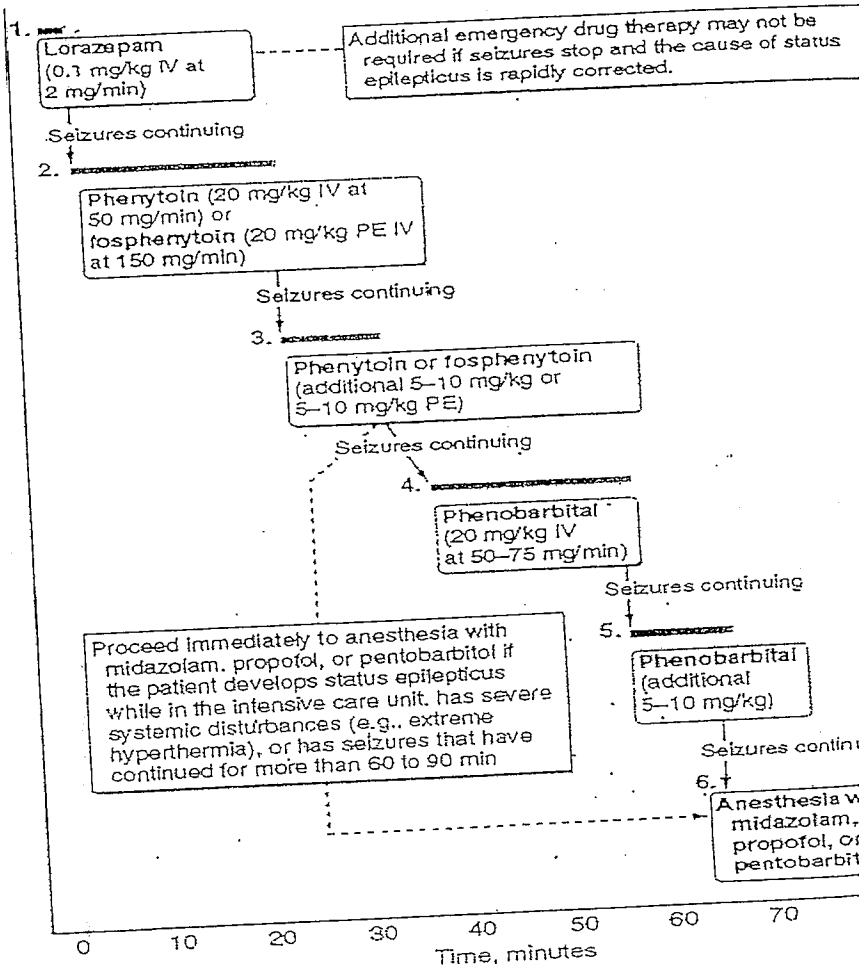
Etiology → Anticonvulsant noncompliance.
→ Same causes of seizure [especially hypoglycemia & electrolyte disorders]

Management

- ABC: Airway, Breathing, & Circulation and once IV line is established administer 50 mL 50% dextrose in water, 100 mg thiamine, and 0.4 mg naloxone.
- Send ***Investigations*** → For the cause: Glucose, Electrolytes [Na^{+}, Ca^{++}], Pulse oximetry, ABG, LFTs, Urea/Creatinine & CBC, ESR, Toxicology screen.
  → Defer EEG and brain imaging until the pt is stabilized.
  → If pt is has fever or meningesm signs → LP [if no contraindications]

- Treatment
  - 1st drug: diazepam or lorazepam:
  - Diazepam is given IV or rectally
  - Lorazepam is given IV

- If seizures continues after 30-60 mins → Anesthesia



Raised intracranial pressure

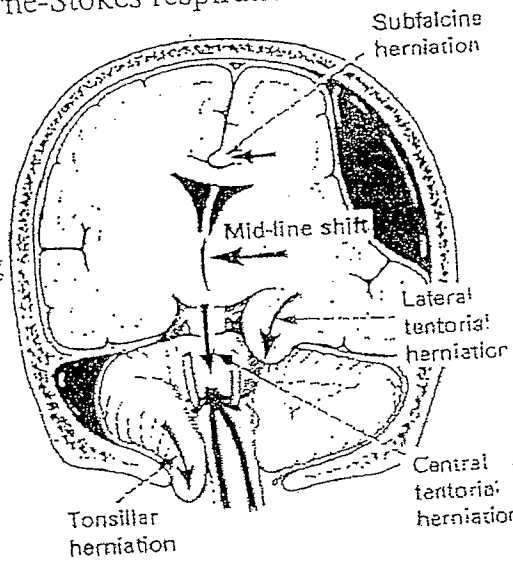
Definition:

Causes = Differential diagnosis:

1. Head trauma → Epidural hematoma
   → Subdural hematoma
2. Tumors
3. Intracerebral hemorrhage or Subarachnoid hemorrhage.
4. Infection (Meningitis)
5. Idiopathic [Pseudotumor cerebri]

Clinical presentation

- Headache (worse upon awakening & ↑ by coughing & bending forward)
- Nausea, vomiting.
- Papilledema → blurred vision
- Diplopia due to 6th CN nerve or 3rd CN palsy.
- **Cushing Triad**: Bradycardia + Hypertension + Cheyne-Stokes respiration
- ↓ level of consciousness & coma
- ↑ ICP can lead to Herniation syndromes which are:
  - *Subfalcine herniation*: Medial cortex moves under the midline falx → obstructs anterior cerebral artery.
  - *Uncal herniation*: Uncus displaced through tentorium, compressing 3rd CN [ipsilateral] & pushing the cerebral peduncle → Contralateral hemiparesis
  - *Tonsiller herniation*: Cerebellar tonsils displaced into the foramen magnum causing medullary compression → cardiorespiratory arrest.



False localizing signs[dysfunction distant from the expected anatomical site] :

- Pupillary dilatation (ipsilateral to lesion)
- Hemiparesis (ipsilateral to lesion)
- 6th cranial nerve lesion (unilateral or bilateral)

Treatment

1. Elevate head of the bed
2. Mannitol
3. Glucocorticoids—dexamethasone
4. Hyperventilation—to $PaCO_2$ 30–35 mmHg
5. Sedation (e.g., morphine, propofol, or midazolam)

Meningitis

Definition: An acute infection of the meninges

Epidemiology

- Commonest in pediatric age but may occur at any age.
- Gender: Males = Females.

Risk factors

- Infection at any part in the body [pneumonia, sinusitis, otitis media]
- Impaired immunity (Alcoholism, Diabetes, HIV)
- Splenectomy
- Head trauma and neurosurgery

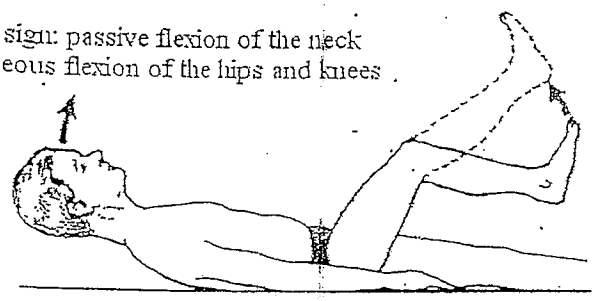
Etiology

- Viral infection is the most common cause of meningitis. [e.g. EBV, HS, HZ]
- Streptococcus pneumonia [most common bacterial cause in adults]
- N. meningitides [2nd most common bacterial cause]
- H. Influenza
- Tuberculosis
- In Pediatrics [E. coli, Group B streptococci, Listeria monocytogenes]

Clinical features

- **Headache**
- Photophobia
- Constitutional symptoms: **Fever**, malaise, anorexia.
- **Nuchal rigidity (Stiff neck)** : neck resists passive flexion.
- Signs of Meningeal irritation:
  - ***Kernig's sign:*** pt in supine position and with hip & knee are flexed: on passive extension of the knee will → spasm hamstring ms
  - ***Brudzinski's sign:*** with pt in the supine position: on passive flexion of the neck will → spontaneous flexion of the hips and knees.

Brudzinski's sign: passive flexion of the neck will spontaneous flexion of the hips and knees



Kernig's sign: stretching nerve roots by extending the knee causes pain.

Note: The presence of Purpuric Rash suggests meningococcemia.

Investigation

Lumbar puncture with CSF analysis if no contraindications are present

CSF analysis			
	Bacterial	**Viral**	**TB meningitis**
Appearance	Turbid	Clear	Clear
Cells (per mm^3)	> 2000	> 500	> 1000
Main cell type	Neutrophil	Lymphocyte	Lymphocyte
Glucose (mM)	Very low	Normal	Low
Protein (g/L)	↑↑↑	Normal or ↑	↑↑↑
Other tests	Gram stain Bacterial antigen	PCR	Ziehl-Neelsen Fluorescent test PCR

Treatment

- Bacterial meningitis:
  - Empirical with: IV 3rd **generation cephalosporins + Vancomycin** OR **Rifampicin**
  - If there is purpuric rash [meningococcal]: IV Benzylpenicillin
  - **Dexamethasone** should be given 20 minutes before antibiotics to prevent the development of adhesion and therefore hydrocephalus.
  - Rifampin prophylaxis for close contacts of pts with meningococcal disease.
- Viral meningitis: self-limiting & treatment is supportive
- TB meningitis: Anti-TB + Corticosteroids

Complications

- Hydrocephalus
- Epilepsy
- Septicemia
- Deafness in children is associated with H. influenza infection [↓ by giving corticosteroid to children]

Idiopathic Benign Intracranial Hypertension (Pseudotumor Cerebri)

Etiology: Idiopathic but may be due to ↓ in CSF reabsorption by the arachnoid vill

Epidemiology: Middle age Obese Female.
Associations: OCP, Steroids withdrawal, Adison's disease, Vit A, Vit D, Tetracycline.

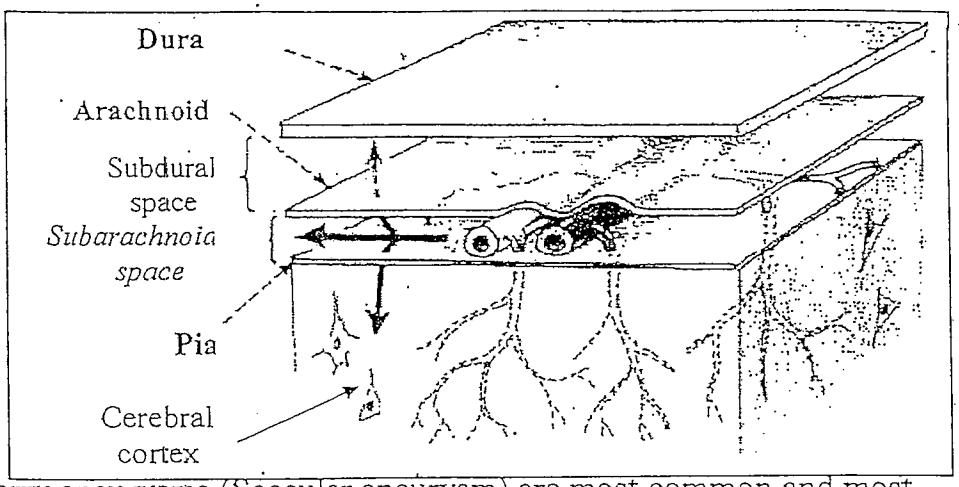
Clinical feature: As above

Investigation: It is the diagnosis of exclusion [CT & MRI of the brain shows no mass and no dilatation of ventricles] CSF is normal except for increased pressure.

Treatment: Wight reduction Acetazolamide or therapeutic Lumbar Puncture.

Subarachnoid Hemorrhage (SAH)

Definition: An acute hemorrhage into the subarachnoid space (where intracranial vessels are present)



Epidemiology

- Gender: ♀> ♂
- Age > 20 yrs

Etiology

- Aneurysms:
  - Congenital Berry aneurysms (Saccular aneurysm) are most common and most common site is junction of posterior communicating & internal carotid arteries
  - Risk factors for aneurysm: •Old age • Atherosclerosis • +ve family history • Adult polycystic kidney disease (APCKD) • Ehlers-Danlos syndrome
- Trauma
- Ateriovenous malformation

Clinical features: Any of the following:

- Sudden onset of **Severe explosive** (Thunderclap) **headache** ± Vomiting
- **Meningism**: meningitis signs but not due to meningitis [Neck stiffness. Photophobia] develop after 3-12 hours
- Loss of consciousness [coma] OR Epilepsy
- Accumulation of blood → intracerebral hematoma →**Hemiparesis**
- Aneurysm of the posterior communicating artery → 3rd CN palsy

Investigations

- Immediate head **non-contrast CT**
- If CT is negative → Immediate **LP** : shows RBCs or **Xanthochromia** [yellowish CSF due to breakdown of RBCs it occurs 6 hrs after the onset of headache]
- **Angiography** should be performed once SAH is confirmed.
- **ECG:** may show ST segment depression

Treatment

- Calcium channel blockers (Nimodipine) is given acutely to prevent spasm
- Treat headache with paracetamol and codeine. Don't treat hypertension if present
- Treat **↑ICP if present** and give **Seizure prophylaxis.**
- Call neurosurgery: treatment either open clipping or endovascular coiling

Prognosis: Immediate mortality about 30%. Re-bleed rate is about 40% in first 4 wks

Miscellaneous

CSF Analysis

Indications

1-Diagnostic

- Suspicion of meningitis: ↑ cells and proteins
- Suspicion of subarachnoid hemorrhage: Clear blood or Xanthochromia
- Guillain-Barré syndrome: Only elevated proteins
- Multiple sclerosis: Oligocloncal bands

2-Therapeutic

- Therapeutic relief of pseudotumor cerebri
- Infusion of anesthetic, chemotherapy [Methotrexate in ALL]

Contraindications

- Infected skin over the needle entry site
- Increased intracranial pressure including papilledema
- Low platelets or Coagulation problem
- Brain abscess
- Uncooperative pt

Coma

Definition: Coma is a state in which a pt is unresponsive to environmental stimuli and unable to communicate in any manner.

Etiology

1. Metabolic → Systemic failure: **Respiratory**, Liver, Renal, Hypothyroidism
   → DM [**Hypoglycemia**, DKA, Hyperglycemic Hyperosmolar coma]
   → Hypo or hypernatremia, Acidosis, Hypothermia
   → **Thiamin deficiency [Wernicke's encephalopathy]**
   → Drugs & Toxins: **Opioids**, Alcohol, Orgnaophosphate
2. Trauma
3. Tumor
4. Infection: Meningitis, Encephalitis, Brain abscess, Generalized sepsis
5. Infarction: Cerebral, Brainstem, SAH

Approach to pt

History → Any complains before the coma [e.g. headache neck stiffness]
→ PMH about any systemic disease. [Resp, CVS, Renal, Endo]
→ Drug history

Examination → Assess for Glasgow-coma scale
→ Pupils → Pin-point : • **Pontine hemorrhage** • Opiates overdose
• Organophosphate poisoning
→ Large nonreactive : • CN III palsy • Barbiturate overdose

Treatment: ABC

Coma cocktail: Oxygen + 50 mL 50% dextrose + 100 mg thiamine + 0.4 mg Naloxone

Definitive treatment will depend on the cause

Wernicke's encephalopathy: a condition occurs in ch. alcoholics due to Thiamin def and characterized by = *horizontal nystagmus* + *ophthalmoplegia* (due to weakness of one or more extraocular muscles) + *cerebellar ataxia* + *mental impairment*
If there is also *psychosis* it is called *Wernicke-Korsakoff syndrome*

Pontine hemorrhages: hemorrhage occurring in the pons, typically in hypertensive pts it causes deep coma with quadriplegia usually occurs over a few minutes. Pupils are pin-point" (1 mm) pupils and react to light. Death often occurs within a few hours, but small hemorrhages are compatible with survival.

Organophosphate poisoning

Organophosphates irreversibly inhibit acetylcholinesterase and cause accumulation of acetylcholine at muscarinic and nicotinic synapses.

Clinical manifestations [SLUDGE]

- Salivation •Lacrimation •Urination •Defecation •GIT:.nausea vomiting • Eye: miosis.
- Muscle Cramps
- Vital signs: Bradycardia, Hypotension, Respiratory depression,
- Confusion, and coma may result

Treatment

- Treatment begins with washing exposed surfaces with soap and water and,
- In cases of ingestion, GI decontamination, then activated charcoal.
- Atropine IV for symptoms
- Pralidoxime IV to break the bond between organophosphate & cholinesterase enz

↳ given early as soon as you can [best in 1st 6 hours b/c it will be irreversible after 48 hours

Respiratory diseases					
	Asthma	Ch. Bronchitis	Emphysema	Bronchiectasis	ILD
Def	Ch. inflamm. airway disease chara. by episodes of reversible airway bronchospasm	Presence of productive cough for ` months/yr in 2 successive years	Permanent destruction of alveolar wall	Permanent destruction & dilation of bronchi	Group of diseases characterized by fibrosis in the ... ...erstitium.
Cause	Gene+ Environment	Smoking	Smoking	Acquired infection [TB] or Genetic [Cystic fibro]	Idiopathic, Sarcoidosis, Pneumoconiosis
C/P	Wheeze + Cough + Dyspnea	Wheeze + Productive Cough ± Dyspnea	Wheeze + Dyspnea ± Cough	Cough productive of large amount of sputum	Exertional dyspnea & dry cough
PFT	Obstructive	Obstructive	Obstructive	Obstructive	Restrictive
CXR	Hyperinflated chest	Hyperinflated chest	Hyperinflated chest	Hyperinflated chest	Reticulonodular shadow
Ix	Reversibility on bronchodilator	Not reversible on bronchodilator	CT scan	CT scan	CT scan
Resp.F	Type 1	Type 2	Type 1	Type 1	Type 1
Rx	Bronchodilator + Corticosteroids	Stop smoking + Bronchodilator + Corticosteroids & antibiotic on exacerpation	Stop smoking + Bronchodilator	Physiotherapy + Bronchodilator + Antibiotic + Mucolytic	Corticosteroids